

protein derived from this enzyme, by suppression, addition or substitution of at least one amino acid, the said enzyme or derived protein having the property of migrating to the sites of biosynthesis of the starch granules in plant cells and of attaching to the starch granules, the said nucleotide sequence coding for the enzyme or aforementioned protein being positioned upstream of a nucleotide sequence coding for a peptide or polypeptide of interest.

Claim 2 (amended) A recombinant nucleotide sequence of Claim 1, wherein the nucleotide sequence coding for a starch synthase, or for a derived protein, codes for the starch synthase bound to the starch granule or GBSS present in plants, algae or micro-algae.

Claim 3 (amended) A recombinant nucleotide sequence of Claim 1 wherein the nucleotide sequence coding for a starch synthase, or for a derived protein, is selected from the group consisting of

- the nucleotide sequence SEQ ID NO : 1 of the cDNA coding for the GBSSI of *Chlamydomonas reinhardtii*,

- or a fragment of the nucleotide sequence SEQ ID NO : 1. shown in which the nucleotide of the 5' end corresponds to that located in one of the positions 1 to 186 of SEQ ID NO : 1, and in which the nucleotide of the 3' end corresponds to that located in one of the positions 1499 to 3117 of SEQ ID NO : 1.

Claim 4 (amended) A recombinant nucleotide sequence of

Claim 1, wherein the nucleotide sequence coding for a peptide or polypeptide of interest is selected from the group consisting of

- those encoding biologically active peptides, especially peptides of therapeutic interest or that can be used in the agricultural and food industry, and
- those encoding enzymes that are able to transform starch.

Claim 5 (amended) A recombinant nucleotide sequence of Claim 1, wherein it contains a nucleotide sequence encoding a cleavage site, the said nucleotide sequence being positioned between the nucleotide sequence coding for a starch synthase, or a protein derived from the latter, and the nucleotide sequence encoding the polypeptide of interest.

Claim 6 (amended) A transgenic plant cell selected from the group consisting of cells of plants, algae and micro-algae, that are able to produce starch, the said cells containing a recombinant nucleotide sequence of Claim 1 integrated in its genome or maintained in a stable manner in its cytoplasm.

Claim 7 (amended) A member of the group consisting of transgenic plants, algae, micro-algae, flowers, fruits, leaves, stems, roots, seeds, and fragments of these plants, algae or micro-algae, containing a recombinant nucleotide sequence of Claim 1 integrated in the genome or maintained in a stable manner in the cytoplasm of the cells of which they are composed.

Claim 8 (amended) A fusion polypeptide, containing

- in the N-terminal position, a starch synthase, or a protein derived from this enzyme, especially by suppression, addition or substitution of one or more amino acids, the said starch synthase or derived protein having the property of migrating to the sites of biosynthesis of the starch granules in plant cells and of attaching to the starch granules,

- and, in the C-terminal position, a peptide or polypeptide of interest,

the C-terminal part of the amino acid sequence of the starch synthase, or of the derived protein, thus being bound to the N-terminal part of the peptide sequence of interest, the said fusion polypeptide being encoded by a recombinant nucleotide sequence of Claim 1.

Claim 9 (amended) A fusion polypeptide of Claim 8, wherein the starch synthase is selected from the group consisting of

- the peptide sequence SEQ ID NO : 3 corresponding to the GBSSI of *Chlamydomonas reinhardtii* in the form of pre-protein of 708 amino acids,

- or a fragment of the peptide sequence SEQ ID NO : 3, wherein the sequences in which the amino acid of the amino terminal end corresponds to that located in one of the positions 1 to 58 of SEQ ID NO : 3, and in which the amino acid of the carboxy terminal end corresponds to that located in one of the positions 495 to 708 of SEQ ID NO : 3 selected from the group consisting of

• the sequence SEQ ID NO : 5 corresponding to the GBSSI of *Chlamydomonas reinhardtii* in the form of mature protein of 651 amino acids,

- the sequence SEQ ID NO : 7 corresponding to a fragment of 438 amino acids of the peptide sequence of the GBSSI of *Chlamydomonas reinhardtii*,

• the sequence SEQ ID NO : 9 corresponding to a fragment of 531 amino acids of the peptide sequence of the GBSSI of *Chlamydomonas reinhardtii*,

- and a peptide sequence derived from an aforementioned peptide sequence or fragment, by substitution, suppression or addition of at least one amino acid, and having the property of attaching to the starch granules, the said derived peptide sequence preferably having a homology of at least about 60%, with the aforementioned peptide sequence or fragment.

Claim 10 (amended) A fusion polypeptide of Claim 8 wherein it contains a cleavage site positioned between, on the one hand, the starch synthase, or a protein derived from the latter, and, on the other hand, the polypeptide of interest.

Claim 11 (amended) A starch granule, containing at least one fusion polypeptide of Claim 8.

Claim 12 (amended) A pharmaceutical composition comprising a starch granule containing at least one fusion polypeptide of Claim

8 and a physiologically acceptable vehicle, the peptide of interest in the said fusion polypeptides possessing a defined therapeutic effect.

Claim 13 (amended) A pharmaceutical composition of Claim 12, wherein the diameter of the starch granules is between about 0.1  $\mu\text{m}$  and several tens of  $\mu\text{m}$ , and the proportion by weight of the fusion polypeptides in these granules is between about 0.1% and 1%.

Claim 14 (amended) A pharmaceutical composition, containing at least one fusion polypeptide of Claim 8 and a physiologically acceptable vehicle, the peptide of interest in the said fusion polypeptides possessing a defined therapeutic effect.

Claim 15 (amended) A food composition containing starch granules of Claim 11, the peptide of interest in the said fusion polypeptides being usable in the food-processing field.

Claim 16 (amended) A method of preparation of starch granules of Claim 11, comprising

- transformation of plant cells, by means of a cellular host, or transformed by a recombinant vector, containing a recombinant nucleotide sequence of Claim 1,

- obtaining plants, algae or micro-algae transformed so that their genome contains at least one or more nucleotide sequences of

Claim 1, by *in vitro* culture of the aforementioned transformed host cells,

- optionally fertilization and recovery of the seeds of the plants obtained in the preceding stage, and cultivation of these seeds to obtain plants of the next generation and

- extraction of the starch granules from a member of the group consisting of the plants, algae or micro-algae, flowers, fruits, leaves, stems, roots, or fragments of these aforementioned transformed plants, algae or micro-algae.

Claim 17 (amended) A method of preparation of fusion polypeptides of Claim 8 by the method of Claim 16 comprising an additional stage of recovery, and optionally, purification of the fusion polypeptides from the starch granules.

Claim 18 (amended) A method of preparation of a peptide by the method of Claim 16 by transformation of host cells with the nucleotide sequences of Claim 5, and includes an additional stage of cleavage of the fusion polypeptide obtained, by means of a suitable reagent, then, optionally, a stage of purification of the polypeptide of interest.

Claim 19 (amended) A method of biotransformation of starch granules, comprising

- transformation of plant cells by means of a cellular host, or transformed by a recombinant vector, containing a

recombinant nucleotide sequence of Claim 4, encoding enzymes that are able to transform starch,

- obtaining plants, algae or micro-algae transformed so that their genome contains at least one aforementioned nucleotide sequence, by *in vitro* culture of the aforementioned transformed host cells,

- optionally, fertilization and recovery of the seeds of the plants obtained in the preceding stage, and cultivation of these seeds to obtain plants of the next generation,

- extraction of the starch granules from a member of the group consisting of the plants, algae, micro-algae, flowers, fruits, leaves, stems, roots, or fragments of these aforementioned transformed plants, algae or micro-algae,

- optionally heating of the said starch granules to a temperature at which the peptide of interest of the fusion polypeptide is capable of being active.

PLEASE ADD THE FOLLOWING CLAIMS:

--20. A recombinant nucleotide sequence of Claim 3 selected from the group consisting of

- the sequence SEQ ID NO : 2 coding for the GBSSI of *Chlamydomonas reinhardtii* in the form of pre-protein of 708 amino acids (SEQ ID NO : 3),

- the sequence SEQ ID NO : 4 coding for the GBSSI of *Chlamydomonas reinhardtii* in the form of a mature protein of 651

amino acids (SEQ ID NO : 5),

- the sequence SEQ ID NO : 6 coding for a fragment of 438 amino acids (SEQ ID NO : 7) of the GBSSI of *Chlamydomonas reinhardtii*,

- the sequence SEQ ID NO : 8 coding for a fragment of 531 amino acids (SEQ ID NO : 9) of the GBSSI of *Chlamydomonas reinhardtii*,

- a nucleotide sequence derived by degeneration of the genetic code of the aforementioned nucleotide sequences, and coding for the aforementioned GBSSI of *Chlamydomonas reinhardtii*, or for an aforementioned peptide fragment of the latter,

- a nucleotide sequence derived from a nucleotide sequence or fragment mentioned above, especially by substitution, suppression or addition of one or more nucleotides, and coding for a peptide sequence derived from the aforementioned GBSSI of *Chlamydomonas reinhardtii*, or derived from an aforementioned peptide fragment of the latter, and having the property of attaching to the starch granules, the said derived nucleotide sequence preferably having a homology of at least about 50%, and preferably of at least about 70%, with the aforementioned nucleotide sequence or fragment,

- and a nucleotide sequence capable of hybridizing with one of the aforementioned nucleotide sequences or fragments.

21. A sequence of Claim 4 wherein the enzyme is one that